Endoscopic Features of Patients with Bronchial Asthma and Gastroesophageal Reflux Symptoms

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ABSTRACT

***Background**: Studies evaluating endoscopic results in patients with bronchial asthma and Gastroesophageal Reflux Disease (GERD) in Gatot Soebroto hospital have never been undertaken. It leads an idea to further study, in order to find a more accurate and rapid management as solution for anticipating asthma attack and complications of bronchial asthma to upper gastrointestinal tract.*

***Methods**: A retrospective study was aimed to evaluate endoscopic result of upper gastrointestinal tract in bronchial asthma patients who had GERD symptoms as appropriate to the criteria of 4 major GERD symptoms of Talley 2002. Data was collected in one year period starting from November 2004 to October 2005.*

***Results**: Subject characteristics in this study indicated that there were more female patients compared to male with a ratio approaching 3:1 who had such symptoms. Mean age was 38.5 years and ratio of body weight to body height indicated normal weight result and the mean value for duration of asthma was 27 years. Clinical symptoms of GERD found in the present study was in accordance with four majors symptoms of GERD i.e. 32 (100.00%) cases of regurgitation, 29 (90.63%) cases for each of heartburn and non-cardiac chest pain symptom, and 7 (21.88%) cases of difficult / painful swallowing or dys/ odinophagia. The endoscopic result of upper gastrointestinal tract had figured of: (1) 4 (12.50%) cases of normal esophagus, (2) 11 (34.40%) cases of non-erosive esophagitis known as Non Erosive Reflux Disease (NERD), and (3) erosive esophagitis which regarding to Los Angeles classification: 15 (46.90%) cases of grade A and 2 (6.20%) cases of grade B.*

***Conclusion**: The incidence of esophagitis in accordance with LA classification is extremely high although no severe damage (grade C and grade D) was found. Early anticipation of reflux associated respiratory symptoms and anti-reflux treatment should be considered in order to shorten or to discontinue the asthma attack cycle.*

***Keywords**: bronchial asthma, GERD, endoscopy, NERD*

INTRODUCTION

Bronchial Asthma (BA) is a chronic inflammation disorder of respiratory tract involving various inflammation cells. BA symptoms may be induced by various stimulants including reflux gastroesophageal or known as Reflux Associated Respiratory Symptoms (RARS).[1] The Gastroesophageal Reflux Disease (GERD) is defined as symptoms or esophageal mucosa damage (esophagitis) due to abnormal reflux of gastric component into esophagus.[2-4] Esophageal reflux has strongly associated with several symptoms and respiratory tract disorder including chronic cough (bronchitis) and BA.[5] The first person came with an idea of an association between GERD and BA was William Osler, and he stated that an asthma attack is possibly caused by direct irritation on mucosa of bronchus or indirectly by gastric refluxate effect.[6-9] The prevalence between GERD and BA is unknown, but it is predicted between 34-89%.[7,10-12] Several studies had described that 55-82% of asthma patients have GERD symptoms.[9,10,12-14] The endoscopic results of asthma patients have shown that the prevalence of

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esophagitis is in range of 27-43%.[7,11-15] Previous studies have demonstrated that anti-reflux drugs therapy decrease asthma symptoms and it has minimal or zero effect to the lungs.[16] Esophagitis is caused by recurrent gastric refluxate on distal esophagus which bring an effect and causing inflammation of esophageal mucosa. This condition is known as reflux esophagitis or GERD.[17] In addition, gastroesophageal reflux may be facilitated by asthma bronchial drugs.[9-12,14] In spite of the histopathologic etiology, reflux esophagitis may be divided to Non Erosive Reflux Disease (NERD) and erosive reflux disease.[17]

GERD cases and its association with BA have never been studied at the Gatot Soebroto hospital. In contrast, there are number of BA cases found at outpatient clinic of Gastroentero-hepatology Division, Department of Internal Medicine, Gatot Soebroto hospital, with heartburn/pyrosis symptom, non-cardiac chest pain, regurgitation, difficult/painful swallowing or dys-/odinophagia. Those symptoms may appear s imultaneously or consecutively. Moreover, many patients that had been referred from outpatient clinic of Pulmonology Division, Gatot Soebroto hospital or beyond hospital - had experienced gastrointestinal endoscopy in order to confirm their diagnosis, but somehow it was never came to an idea of considering its association with asthma bronchial. Those symptoms were known as reflux type of dyspepsia, which further in the late 1990's known as Gastroesophageal Reflux Disease (GERD).[18] On Asia-Pacific Digestive Week (APDW) in Bali, Talley (2002) had classified those symptoms as "Four Mayor Symptoms of GERD".[18]

Endoscopic evaluation in RARS cases is less conducted. A study report by Department of Pulmonology and Respiratory Medicine, Faculty of Medicine, University of Indonesia, Jakarta (2005) had concluded that there were 52.8% cases of reflux associated respiratory symptoms (RARS).[19] This finding leads to a question as also a title on this study, on what can be drawn as endoscopic features of patients with BA and GERD syndrome. The present study was aimed to collect data about the prevalence of upper gastrointestinal tract disorder in patients with BA and clinical symptoms of GERD.

METHODS

A retrospective study was conducted by examining data of endoscopic results in patients with BA who also had symptoms in keeping with GERD. Subjects were referred patients by Division of of Pulmonology, Department of Internal Medicine, Faculty of Medicine, University of Indonesia, who were subsequently sent to Division of Gastroentero-hepatology, Department of Internal Medicine, Gatot Soebroto hospital during one year period (November 2004 to October 2005). The inclusion criteria were: (a) patient with moderate persistent asthma bronchial (in accordance with the referred diagnosis); (b) patient who has one or more ($\geq$ 1) major GERD symptom(s) of Talley's criteria; (c) range of age between 13-65 years; (d) attached with complete data of macroscopic endoscopy result (provided at gastrointestinal endoscopic area at Department of Internal Medicine of Gatot Soebroto hospital) and microscopic result (i.e. pathology anatomy result). The exclusion criteria were: (a) identified fungus, polyp, tumor, and upper gastrointestinal tract bleeding, and (b) incomplete data. Statistical assessment was performed by using t-test in SPSS version 13.0 for windows.

Data was collected from reported endoscopic results in BA patient with GERD symptoms and pathology anatomy (histopathologic) results. The instrument used for gastrointestinal endoscopy in the present study was a set of endoscopy by Olympus EVIS GIF type 130 front-view. It was conducted in accordance with Standard Operational Procedure (SOP) at gastro-intestinal endoscopic area, Department of Internal Medicine at Gatot Soebroto hospital. The present study was conducted on: (a) data collection which included endoscopic results of upper gastrointestinal tract (EGD = esophagogastro-duodenoscopy) by using endoscopic instrument of Olympus EVIS GIF type 130 front-view (1996), and reported data of histopathologic results as classified in criteria of inclusion; (b) classification and clarification; (c) analysis and discussion; (d) data of statistical result. Reported data was resumed and concluded.

RESULTS

The results of retrospective study were clarified and classified into: (1) patient characteristics, (2) clinical symptoms of BA patient with GERD, (3) endoscopic results of upper gastrointestinal tract (macroscopic result), and (4) histopatologic results (histopathologic, microscopic result).

During one year period (November 2004 to October 2005), we have collected 36 subjects of BA patients with GERD under endoscopic treatment of upper gastrointestinal tract. Four subjects then were excluded due to incomplete data. The remained 32 subjects were classified based on: sex distribution, age, body height/weight, and duration of illness for BA, as seen in table 1. The results were found as follows: 9 male subjects (28.12%) and 23 female subjets (71.88%). Range of age was between 18-59 years (mean 38.5). Mean of body height/weight 156.47 cm/58.9 kg. Duration of illness for BA was between 4-50 years.

Table 1. Characteristics of patients with bronchial asthma and GERD symptoms who had experienced endoscopic treatment of upper gastrointestinal tract

Characteristic	Number	
Sex		
Male	9 subjects	(28.12%)
Female	23 subjects	(71.88%)
Age	18-59 years	(mean 38.5 years)
Body height/weight (cm/kg)	156.47/58.9	(normoweight)
Duration of illness for BA	4-50 years	mean of 27 years

The clinical symptoms that clarified in accordance with 4 major Talley criteria were as follows (table 2): heartburn in 29 subjects, non-cardiac chest pain in 29 subjects, regurgitation in 32 subjects, and difficult/painful swallowing or dysphagia/odinophagia in 7 subjects. The symptoms might appear consecutively or simultaneously with the 3 others, or possibly appeared with other dyspepsia symptoms. However, authentic dyspepsia symptom was not recorded on patient's data. Thus, it can not be clarified or classified.

The esophagogastroduodenoscopic (EGD) results of Bronchial Asthma (BA) patients with Gastroesophageal Reflux Disease (GERD), is shown on table 3.

Table 2. Clinical symptoms in patients with bronchial asthma patient and GERD symptoms in accordance with Talley criteria

Four mayor symptoms of GERD	1	2	3	4	% Dominant
Regurgitation	32	-	-	-	100.00%
Heartburn	-	29	3	-	90.63%
Non-cardiac chestpain	-	3	29	-	90.63%
Dys/Odinophagia	-	-	-	7	21.88%

Table 3. EGD results in bronchial asthma patients with GERD symptoms

Endoscopic features	Number of patients	%
Normal mucosa		
- Authentic	4	12.5
- With other upper gastrointestinal tract disorders	0	-
Non erosive Esophagitis		
- Authentic	5	15.60
- With other upper gastrointestinal tract disorders	6	18.80
Erosive esophagitis grade A		
- Authentic	7	21.90
- With other upper gastrointestinal tract disorders	8	25.00
Erosive esophagitis grade B		
- Authentic	1	3.10
- With other upper gastrointestinal tract disorders	1	3.10
Erosive esophagitis grade C	0	-
Erosive esophagitis grade D	0	-
With other upper gastrointestinal tract disorder, i.e.:	15	6.9
- Hyperemetic gastropathy	5	15.60
- Erosive gastropathy	3	9.30
- Ulcerative gastropathy	2	6.20
- Gastric ulcer	1	3.10
- Biliary reflux	3	9.30
- Herniation of gastric body	1	3.10

Table 4. Histopathological result of esophageal mucosa tissue biopsy in bronchial asthma patients with GERD symptoms

Histopathological test	Amount	%
Not performed	2	6.25
Less representative	2	6.25
Identified as mild chronic esophagitis	28	87.50

DISCUSSION

There are more frequent BA patients with GERD symptoms in female compared to the male, with comparison of 23.9 or almost 3:1. Mean age is 38.5 years (productive age), the body posture is within normal limits (normoweight), and duration of BA illness is > 25 years. Such demographic data has never been reported previously in other study. Endoscopic examination in patients with BA is performed based on following indications, i.e. identified at least one of 4 major symptom (Talley, 2002) and gastroesophageal reflux disease. The symptoms are classified into: regurgitation (100%), heartburn (90.63%), non-cardiac chest pain (90.63%), and difficult/painful of swallowing or dysphagia/odinophagia (31.88%). This frequency of symptoms is actually higher Talley report

Based on the study results, we may consider that the incidence of GERD is higher in patients with BA compared to the non-BA. Gastric acid are the most strongly affecting refluxate and the incidence of esophagitis may reach to 22.8%.[20] Some experts demonstrated that reflux of gastric acid into esophagus is facilitated by several predisposition factors due to BA treatment such as autonomic dysregulation of lower esophageal sphincter,[21] tonus gradient of thorax-abdominal cavity, airway obstruction that cause high prevalence of hiatal hernia and dysfunction of crus diaphragm, consuming asthma drugs (bronchodilators, teophyline, salbutamol, prednisone).[9,11-14,21,22]

In contrast, GERD may also stimulate bronchial asthma. The pathophysiology includes broncho-constriction, such as dysfunction of vagal reflex of esophagus and bronchus, bronchus hyper-responsiveness, and microaspiration of gastric acid into respiratory tract.[12,21-23] In addition, it may also caused by neurogenic inflammation reaction of nociceptive substances at afferent sensory nerves of esophageal mucosa, i.e.release of tachykinin substances (neurotransmitter) which induce larynx and lower respiratory tract and produce cough, broncho-constriction, and mucosa edema.[24] The process is known as axon reflex.[25]

The macroscopic features of esophageal mucosa in patients with BA and GERD symptoms can be seen by endoscopic examination of upper gastrointestinal

tract (macroscopic: by endoscopy). According to Los Angeles classification (1996), erosive esophagitis by endoscopic examination are classified into 4 grades, i.e. Grade A, B, C and D.[26] In clinical situation, it is known as: non-erosive esophagitis, erosive esophagitis of grade A and B that are considered as mild esophagitis and others as moderate esophagitis. Severe esophagitis appeared when there is a grade D esophagitis with Barrett's esophagitis, stricture, or complemented by other features of upper gastrointestinal tract disorder. [4,12,18,26]

Of 32 cases that treated with endoscopic examination during a year period (November 2004 to October 2005), there are only 4 cases (12.50%) with authentic normal esophageal mucosa, but the other 28 cases (87.50%) have several degree of esophagitis (non-erosive and erosive), either single/authentic or combined with other upper gastrointestinal tract disorder such as erosive gastropathy and ulcers. It has not been explained yet whether such disorder is caused by treatment of bronchial asthma or on the contrary. However, when 11 cases (34.40%) of non-erosive esophagitis and 17 cases of erosive esophagitis grade A/B (53.10%) are categorized as mild esophagitis which in this study is dominant (87.50%). Therefore, it can be concluded that such endoscopic results are considered as complication of treatment for moderate-persistent BA.

The histopathological results of tissue biopsy from 28 subjects (87.50%) with mild chronic esophagitis have demonstrated a high accuracy precision of endoscopic esophageal mucosa. This finding in accordance with some references stated that endoscopy and biopsy are considered as standard procedures to observe the type and size of tissue damage in reflux esophagitis and it has nearly 100% of sensitivity.[27]

CONCLUSION

In BA patients with GERD symptoms, the clinical symptoms that in accordance with Talley criteria, 2002 are found higher than number of cases which Talley has been concluded previously by himself. The incidence of esophagitis in accordance with LA classification is very high, although no severe damage (grade C and D) are found. Early recognition of Reflux Associated Respiratory Symptoms (RARS) and administration of anti-reflux treatment should be considered in order to shorten/discontinue the asthma attack.

SUGGESTION

It is important to consider reflux associated respiratory symptoms in patients with moderate-persistent bronchial asthma concerning to its effect on esophageal mucosa damages (GERD). It is also necessary to consider administration of anti-reflux treatment (PPI ~ proton-pump inhibitor, or prokinetics, mucosal cytoprotectant) for all cases of bronchial asthma.

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